

## **Annex I**

### **Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)**

## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for tamoxifen, the scientific conclusions are as follows:

In view of available data from the literature on decreased bone mineral density in premenopausal women, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between tamoxifen and decreased bone mineral density in premenopausal women is at least a reasonable possibility. The PRAC concluded that the product information of products containing tamoxifen should be amended accordingly.

In view of available data on prolongation of the QT interval on the electrocardiogram (ECG) from the literature and spontaneous reports, including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between tamoxifen and prolongation of the QT interval on the ECG is at least a reasonable possibility. The PRAC concluded that the product information of products containing tamoxifen should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

## **Grounds for the variation to the terms of the marketing authorisation(s)**

On the basis of the scientific conclusions for tamoxifen the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing tamoxifen is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

## **Annex II**

**Amendments to the product information of the nationally authorised medicinal product(s)**

<Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike-through~~)>

## Summary of Product Characteristics

- Section 4.4

A warning and precaution should be added as follows:

[...]

**Studies in premenopausal women who were treated with tamoxifen for reduction of breast cancer risk or in the management of breast cancer have reported decreases in bone mineral density.**

**Premenopausal women taking <Product name> should be advised regarding measures to maintain bone health, according to local clinical guidelines.**

[...]

A warning and precaution should be added as follows:

[...]

**<Product name> at the recommended dose may prolong the QTc interval on the electrocardiogram (ECG) especially in patients with underlying risks for QT prolongation, including patients with cardiac comorbidities or patients currently treated with other medicinal products known to prolong the QT interval (see section 4.5). ECG and electrolyte monitoring are recommended in such patients.**

[...]

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- Section 4.5

An interaction should be added as follows:

[...]

**<Product name> at the recommended dose may prolong the QTc interval on the electrocardiogram (ECG), and the concomitant use of <Product name> with other medicinal products known to prolong the QT interval may further potentiate QT prolongation. Therefore, caution is advised in case of such combination, and ECG and electrolyte monitoring are recommended in such patients (see section 4.4).**

[...]

- Section 4.8

The following adverse reaction should be added under the SOC 'Musculoskeletal and connective tissue disorders' with a frequency 'not known':

### **Decreased Bone Mineral Density (premenopausal women)**

The following adverse reaction should be added under the SOC 'Cardiac Disorders' with a frequency 'not known':

### **QT prolongation**

- Section 4.9

If similar wording is not already implemented, a warning should be added as follows:

[...]

**There have been reports in the literature that tamoxifen given at several times the standard dose may be associated with prolongation of the QT interval of the ECG.**

## Package Leaflet

- Section 2

A warning and precaution should be added as follows:

### Warnings and precautions

[...]

**Studies in premenopausal women who took tamoxifen for reduction of breast cancer risk or for treatment of breast cancer have reported decreases in bone density. If you are a premenopausal woman undergoing treatment with <Product name>, ask your doctor for advice about ways to maintain your bone health.**

[...]

A warning and precaution should be added as follows:

**If you have any heart conditions including heart rhythm problems (arrhythmia), including a condition called Long QT syndrome (QT interval prolongation), the risk of heart rhythm problems may be increased when using <Product name>**

[...]

### Other medicines and <Product name>

In particular, tell your doctor <or pharmacist> if you are taking any of the following medicines:

[...]

- **Medicines known to affect heart rhythm.**

[...]

### Section 4 . Possible side effects

Not known (frequency cannot be estimated from the available data):

**Decreased bone mineral density in premenopausal women**

**Changes in the electrical activity of the heart (Electrocardiogram QT Prolonged)**

**Annex III**

**Timetable for the implementation of this position>**

### **Timetable for the implementation of this position**

Adoption of CMDh position:	January 2026 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	15 March 2026
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	14 May 2026